

SEQUENCE LISTING

<110> Takeda Chemical Industries, Ltd.

<120> RFRP Receptor Antagonist

<130> 3169W00P

<150> JP 2003-114313

<151> 2003-04-18

<160> 4

<210> 1

<211> 430

<212> PRT

<213> Human

<400> 1

| | | | | | | | | | | | | | | | |
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| Met | Glu | Gly | Glu | Pro | Ser | Gln | Pro | Pro | Asn | Ser | Ser | Trp | Pro | Leu | Ser |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Gln | Asn | Gly | Thr | Asn | Thr | Glu | Ala | Thr | Pro | Ala | Thr | Asn | Leu | Thr | Phe |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Ser | Ser | Tyr | Tyr | Gln | His | Thr | Ser | Pro | Val | Ala | Ala | Met | Phe | Ile | Val |
| | | 35 | | | | 40 | | | | | | 45 | | | |
| Ala | Tyr | Ala | Leu | Ile | Phe | Leu | Leu | Cys | Met | Val | Gly | Asn | Thr | Leu | Val |
| | | 50 | | | | 55 | | | | | 60 | | | | |
| Cys | Phe | Ile | Val | Leu | Lys | Asn | Arg | His | Met | His | Thr | Val | Thr | Asn | Met |
| 65 | | | | 70 | | | | | 75 | | | | | 80 | |
| Phe | Ile | Leu | Asn | Leu | Ala | Val | Ser | Asp | Leu | Leu | Val | Gly | Ile | Phe | Cys |
| | | | 85 | | | | | | 90 | | | | | 95 | |
| Met | Pro | Thr | Thr | Leu | Val | Asp | Asn | Leu | Ile | Thr | Gly | Trp | Pro | Phe | Asp |
| | | | 100 | | | | | | 105 | | | | | 110 | |
| Asn | Ala | Thr | Cys | Lys | Met | Ser | Gly | Leu | Val | Gln | Gly | Met | Ser | Val | Ser |
| | | | 115 | | | | | | 120 | | | | | 125 | |

| | | | |
|---|-----|-----|-----|
| Ala Ser Val Phe Thr Leu Val Ala Ile Ala Val Glu Arg Phe Arg Cys | | | |
| 130 | 135 | 140 | |
| Ile Val His Pro Phe Arg Glu Lys Leu Thr Leu Arg Lys Ala Leu Val | | | |
| 145 | 150 | 155 | 160 |
| Thr Ile Ala Val Ile Trp Ala Leu Ala Leu Leu Ile Met Cys Pro Ser | | | |
| | 165 | 170 | 175 |
| Ala Val Thr Leu Thr Val Thr Arg Glu Glu His His Phe Met Val Asp | | | |
| | 180 | 185 | 190 |
| Ala Arg Asn Arg Ser Tyr Pro Leu Tyr Ser Cys Trp Glu Ala Trp Pro | | | |
| | 195 | 200 | 205 |
| Glu Lys Gly Met Arg Arg Val Tyr Thr Thr Val Leu Phe Ser His Ile | | | |
| | 210 | 215 | 220 |
| Tyr Leu Ala Pro Leu Ala Leu Ile Val Val Met Tyr Ala Arg Ile Ala | | | |
| | 225 | 230 | 235 |
| Arg Lys Leu Cys Gln Ala Pro Gly Pro Ala Pro Gly Gly Glu Glu Ala | | | |
| | 245 | 250 | 255 |
| Ala Asp Pro Arg Ala Ser Arg Arg Arg Ala Arg Val Val His Met Leu | | | |
| | 260 | 265 | 270 |
| Val Met Val Ala Leu Phe Phe Thr Leu Ser Trp Leu Pro Leu Trp Ala | | | |
| | 275 | 280 | 285 |
| Leu Leu Leu Leu Ile Asp Tyr Gly Gln Leu Ser Ala Pro Gln Leu His | | | |
| | 290 | 295 | 300 |
| Leu Val Thr Val Tyr Ala Phe Pro Phe Ala His Trp Leu Ala Phe Phe | | | |
| | 305 | 310 | 315 |
| Asn Ser Ser Ala Asn Pro Ile Ile Tyr Gly Tyr Phe Asn Glu Asn Phe | | | |
| | 325 | 330 | 335 |
| Arg Arg Gly Phe Gln Ala Ala Phe Arg Ala Arg Leu Cys Pro Arg Pro | | | |
| | 340 | 345 | 350 |

Ser Gly Ser His Lys Glu Ala Tyr Ser Glu Arg Pro Gly Gly Leu Leu

355

360

365

His Arg Arg Val Phe Val Val Val Arg Pro Ser Asp Ser Gly Leu Pro

370

375

380

Ser Glu Ser Gly Pro Ser Ser Gly Ala Pro Arg Pro Gly Arg Leu Pro

385

390

395

400

Leu Arg Asn Gly Arg Val Ala His His Gly Leu Pro Arg Glu Gly Pro

405

410

415

Gly Cys Ser His Leu Pro Leu Thr Ile Pro Ala Trp Asp Ile

420

425

430

<210> 2

<211> 432

<212> PRT

<213> Rat

<400> 2

Met Glu Ala Glu Pro Ser Gln Pro Pro Asn Gly Ser Trp Pro Leu Gly

5

10

15

Gln Asn Gly Ser Asp Val Glu Thr Ser Met Ala Thr Ser Leu Thr Phe

20

25

30

Ser Ser Tyr Tyr Gln His Ser Ser Pro Val Ala Ala Met Phe Ile Ala

35

40

45

Ala Tyr Val Leu Ile Phe Leu Leu Cys Met Val Gly Asn Thr Leu Val

50

55

60

Cys Phe Ile Val Leu Lys Asn Arg His Met Arg Thr Val Thr Asn Met

65

70

75

80

Phe Ile Leu Asn Leu Ala Val Ser Asp Leu Leu Val Gly Ile Phe Cys

85

90

95

Met Pro Thr Thr Leu Val Asp Asn Leu Ile Thr Gly Trp Pro Phe Asp

| | | | |
|---|-----|-----|-----|
| 100 | 105 | 110 | |
| Asn Ala Thr Cys Lys Met Ser Gly Leu Val Gln Gly Met Ser Val Ser | | | |
| 115 | 120 | 125 | |
| Ala Ser Val Phe Thr Leu Val Ala Ile Ala Val Glu Arg Phe Arg Cys | | | |
| 130 | 135 | 140 | |
| Ile Val His Pro Phe Arg Glu Lys Leu Thr Leu Arg Lys Ala Leu Phe | | | |
| 145 | 150 | 155 | 160 |
| Thr Ile Ala Val Ile Trp Ala Leu Ala Leu Leu Ile Met Cys Pro Ser | | | |
| 165 | 170 | 175 | |
| Ala Val Thr Leu Thr Val Thr Arg Glu Glu His His Phe Met Leu Asp | | | |
| 180 | 185 | 190 | |
| Ala Arg Asn Arg Ser Tyr Pro Leu Tyr Ser Cys Trp Glu Ala Trp Pro | | | |
| 195 | 200 | 205 | |
| Glu Lys Gly Met Arg Lys Val Tyr Thr Ala Val Leu Phe Ala His Ile | | | |
| 210 | 215 | 220 | |
| Tyr Leu Val Pro Leu Ala Leu Ile Val Val Met Tyr Val Arg Ile Ala | | | |
| 225 | 230 | 235 | 240 |
| Arg Lys Leu Cys Gln Ala Pro Gly Pro Ala Arg Asp Thr Glu Glu Ala | | | |
| 245 | 250 | 255 | |
| Val Ala Glu Gly Gly Arg Thr Ser Arg Arg Arg Ala Arg Val Val His | | | |
| 260 | 265 | 270 | |
| Met Leu Val Met Val Ala Leu Phe Phe Thr Leu Ser Trp Leu Pro Leu | | | |
| 275 | 280 | 285 | |
| Trp Val Leu Leu Leu Leu Ile Asp Tyr Gly Glu Leu Ser Glu Leu Gln | | | |
| 290 | 295 | 300 | |
| Leu His Leu Leu Ser Val Tyr Ala Phe Pro Leu Ala His Trp Leu Ala | | | |
| 305 | 310 | 315 | 320 |
| Phe Phe His Ser Ser Ala Asn Pro Ile Ile Tyr Gly Tyr Phe Asn Glu | | | |

| | | | | | |
|---|-----|-----|-----|-----|-----|
| | 325 | | 330 | | 335 |
| Asn Phe Arg Arg Gly Phe Gln Ala Ala Phe Arg Ala Gln Leu Cys Trp | | | | | |
| | 340 | | 345 | | 350 |
| Pro Pro Trp Ala Ala His Lys Gln Ala Tyr Ser Glu Arg Pro Asn Arg | | | | | |
| | 355 | | 360 | | 365 |
| Leu Leu Arg Arg Arg Val Val Val Asp Val Gln Pro Ser Asp Ser Gly | | | | | |
| | 370 | | 375 | | 380 |
| Leu Pro Ser Glu Ser Gly Pro Ser Ser Gly Val Pro Gly Pro Gly Arg | | | | | |
| 385 | | 390 | | 395 | 400 |
| Leu Pro Leu Arg Asn Gly Arg Val Ala His Gln Asp Gly Pro Gly Glu | | | | | |
| | 405 | | 410 | | 415 |
| Gly Pro Gly Cys Asn His Met Pro Leu Thr Ile Pro Ala Trp Asn Ile | | | | | |
| | 420 | | 425 | | 430 |
| <210> 3 | | | | | |
| <211> 432 | | | | | |
| <212> PRT | | | | | |
| <213> Mouse | | | | | |
| <400> 3 | | | | | |
| Met Glu Ala Glu Pro Ser Gln Pro Pro Asn Gly Ser Trp Pro Pro Ser | | | | | |
| | 5 | | 10 | | 15 |
| Leu Asn Glu Ser Asp Ala Glu Thr Ala Pro Val Ala Ser Leu Thr Phe | | | | | |
| | 20 | | 25 | | 30 |
| Ser Ser Tyr Tyr Gln His Ser Ser Pro Val Ala Ala Met Phe Ile Ala | | | | | |
| | 35 | | 40 | | 45 |
| Ala Tyr Ala Leu Ile Phe Leu Leu Cys Met Val Gly Asn Thr Leu Val | | | | | |
| | 50 | | 55 | | 60 |
| Cys Phe Ile Val Leu Lys Asn Arg His Met Arg Thr Val Thr Asn Met | | | | | |
| | 65 | | 70 | | 75 |
| | | | | | 80 |

| | | | |
|---|-----|-----|-----|
| Phe Ile Leu Asn Leu Ala Val Ser Asp Leu Leu Val Gly Ile Phe Cys | | | |
| | 85 | 90 | 95 |
| Met Pro Thr Thr Leu Val Asp Asn Leu Ile Thr Gly Trp Pro Phe Asp | | | |
| | 100 | 105 | 110 |
| Asn Ala Thr Cys Lys Met Ser Gly Leu Val Gln Gly Met Ser Val Ser | | | |
| | 115 | 120 | 125 |
| Ala Ser Val Phe Thr Leu Val Ala Ile Ala Val Glu Arg Phe Arg Cys | | | |
| | 130 | 135 | 140 |
| Ile Val His Pro Phe Arg Glu Lys Leu Thr Leu Arg Lys Ala Leu Leu | | | |
| | 145 | 150 | 155 |
| Thr Ile Ala Val Ile Trp Ala Leu Ala Leu Leu Ile Met Cys Pro Ser | | | |
| | 165 | 170 | 175 |
| Ala Val Thr Leu Thr Val Thr Arg Glu Glu His His Phe Met Leu Asp | | | |
| | 180 | 185 | 190 |
| Ala Arg Asn Arg Ser Tyr Pro Leu Tyr Ser Cys Trp Glu Ala Trp Pro | | | |
| | 195 | 200 | 205 |
| Glu Lys Gly Met Arg Lys Val Tyr Thr Ala Val Leu Phe Ala His Ile | | | |
| | 210 | 215 | 220 |
| Tyr Leu Ala Pro Leu Ala Leu Ile Val Val Met Tyr Ala Arg Ile Ala | | | |
| | 225 | 230 | 235 |
| Arg Lys Leu Cys Gln Ala Pro Gly Pro Ala Arg Asp Ala Glu Glu Ala | | | |
| | 245 | 250 | 255 |
| Val Ala Glu Gly Gly Arg Ala Ser Arg Arg Arg Ala Arg Val Val His | | | |
| | 260 | 265 | 270 |
| Met Leu Val Met Val Ala Leu Phe Phe Thr Leu Ser Trp Leu Pro Leu | | | |
| | 275 | 280 | 285 |
| Trp Val Leu Leu Leu Leu Ile Asp Tyr Gly Glu Leu Ser Glu Leu Gln | | | |
| | 290 | 295 | 300 |

Leu His Leu Leu Ser Val Tyr Ala Phe Pro Leu Ala His Trp Leu Ala
 305 310 315 320

Phe Phe His Ser Ser Ala Asn Pro Ile Ile Tyr Gly Tyr Phe Asn Glu
 325 330 335

Asn Phe Arg Arg Gly Phe Gln Ala Ala Phe Arg Ala Gln Leu Cys Trp
 340 345 350

Leu Pro Trp Ala Ala His Lys Gln Ala Tyr Ser Glu Arg Pro Gly Arg
 355 360 365

Leu Leu Arg Arg Arg Val Val Val Asp Val Gln Pro Ser Asp Ser Gly
 370 375 380

Leu Pro Ser Glu Ser Gly Pro Ser Ser Gly Val Pro Gly Pro Asn Arg
 385 390 395 400

Leu Pro Leu Arg Asn Gly Arg Val Ala His Gln Asp Gly Pro Arg Glu
 405 410 415

Gly Pro Gly Cys Asn His Met Pro Leu Thr Ile Pro Ala Trp Asn Ile
 420 425 430

<210> 4

<211> 180

<212> PRT

<213> Human

<400> 4

Met Glu Ile Ile Ser Ser Lys Leu Phe Ile Leu Leu Thr Leu Ala Thr
 1 5 10 15

Ser Ser Leu Leu Thr Ser Asn Ile Phe Cys Ala Asp Glu Leu Val Met
 20 25 30

Ser Asn Leu His Ser Lys Glu Asn Tyr Asp Lys Tyr Ser Glu Pro Arg
 35 40 45

Gly Tyr Pro Lys Gly Glu Arg Ser Leu Asn Phe Glu Glu Leu Lys Asp

| | | |
|---|-----|-----|
| 50 | 55 | 60 |
| Trp Gly Pro Lys Asn Val Ile Lys Met Ser Thr Pro Ala Val Asn Lys | | |
| 65 | 70 | 75 |
| Met Pro His Ser Phe Ala Asn Leu Pro Leu Arg Phe Gly Arg Asn Val | | |
| 85 | 90 | 95 |
| Gln Glu Glu Arg Ser Ala Gly Ala Thr Ala Asn Leu Pro Leu Arg Ser | | |
| 100 | 105 | 110 |
| Gly Arg Asn Met Glu Val Ser Leu Val Arg Arg Val Pro Asn Leu Pro | | |
| 115 | 120 | 125 |
| Gln Arg Phe Gly Arg Thr Thr Thr Ala Lys Ser Val Cys Arg Met Leu | | |
| 130 | 135 | 140 |
| Ser Asp Leu Cys Gln Gly Ser Met His Ser Pro Cys Ala Asn Asp Leu | | |
| 145 | 150 | 155 |
| Phe Tyr Ser Met Thr Cys Gln His Gln Glu Ile Gln Asn Pro Asp Gln | | |
| 165 | 170 | 175 |
| Lys Gln Ser Arg | | |
| 180 | | |